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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/332,063	06/14/99	HOLMGREN L	3362-0101P

002292 HM22/0919
BIRCH STEWART KOLASCH & BIRCH
P O BOX 747
FALLS CHURCH VA 22040-0747

EXAMINER	
HARRIS, A	
ART UNIT	**PAPER NUMBER**
1642	14

DATE MAILED: 09/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant
09/332,063	H Imgreen & Troyan vsky
Examiner	**Group Art Unit**
Alana M. Harris, Ph. D.	1642

☒ Responsive to communication(s) filed on *June 22, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1 and 3-33* is/are pending in the applicat

Of the above, claim(s) *9-29* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-8, and 30-33* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 12, filed Feb 23, 2000.

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Claims 1 and 3-33 are pending.

Claim 2 has been canceled.

Claims 3 and 28-30 have been amended.

Claims 31-33 have been added.

Claims 9-29, drawn to non-elected inventions are withdrawn from examination.

Claims 1, 3-8 and 30-33 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

3. Newly submitted claims 28 and 29 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims elected for examination are drawn to a product, an isolated human protein and not methods for treating and manufacturing compositions.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28 and 29 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MEP. § 821.03.

Priority

4. For the application of the art to all examined claims (1, 3-8 and 28-33) are granted the priority date of the Provisional Application #60/089,266 (filed 6/15/98).

Specification

5. The objection to the disclosure because of the following informality: the brief description of the figures lack a separate brief description of Figures 1c, Figure 2a and Figure 2b is withdrawn in view of Applicant's amendment.

Claim Objections

6. The objection of claims 28-30 under 37 CFR 1.75© as being in improper dependent form is maintained. Claim 28 still is improperly multiple dependent because it depends from another multiple dependent claim (claims 3-6), which depend from claim 3. Applicant is advised to state "...any one of claims 1 **or** 3-8...".

Withdrawn Rejections

7. The rejection of claim 30 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is withdrawn in view of Applicants' amendment to the claim.

8. The rejections of claims 1-4 and 28-30 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of Applicants' cancellation and amendments to claims.

9. The rejection of claim 29 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of Applicants' amendment to the claim.

10. The rejection of claim 2 under 35 U.S.C. 102(b) as being anticipated by Petersen et al. (Journal of Biological Chemistry 205(11):6104-6111, 1990) is withdrawn in view of the cancellation of the claim.

New Grounds of Rejection

Claim Rejections - 35 U.S.C. § 112

11. The rejection of claim 1-8 and newly added claims 31-33 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is made and maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 3 is broadly drawn to "...an amino acid sequence having sequence homology equal to or greater than 80% to SEQ ID Nos: 2, 3 or 4 and claims 31-33 are broadly drawn to "...the amino acid sequence has approximately 90% [or 95% or 98%] sequence homology to SEQ ID Nos:2, 3 or 4." The specification while being enabling for the amino acid sequences 2, 3 and 4, which are designated as the proteins "ABP-1" and amino acid variants of ABP-1 that are defined by its ability to bind a fragment of plasminogen, preferably the first four Kringle domains, does not reasonably provide enablement for variants that have at least 80%, 90%, 95% and 98% sequence homology to the recited sequences. Although the Applicants have amended claims 1 and 3 to recite that the protein binds to an N-terminal fragment of plasminogen comprising kringle domains 1-4 and/or 5, there is no guidance as to how to make these divergent sequences, which possess the alleged function. Bork (Genome Research 10:398-400, 2000) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein

level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 bridging paragraph, cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2). Clearly, given the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork the function of the SEQ ID NO:2, 3 and 4 polypeptide could not be predicted, based on sequence similarity with the ABP-1 protein, nor would it be expected to be the same as that of the protein.

Claim Rejections - 35 U.S.C. § 102

12. The rejection of claim 1 and 30 under 35 U.S.C. 102(b) as being anticipated by Petersen et al. (Journal of Biological Chemistry 205(11):6104-6111, 1990) is maintained. Applicants' argue that APB-1 is different from tPA and uPA as ABP-1 in that APB-1 has no enzymatic activity on kringles 1-4 and/or 5 (angiostatin) of plasminogen and that the interaction between ABP-1 and

angiostatin is of the receptor ligand type in that it is merely a binding interaction without a subsequent enzymatic reaction. Likewise the Applicants' state that "..a substantial difference between the uPA and tPA enzymes of the prior art and the ABP-1 receptor of the present invention is the uPA and tPA bind plasminogen in an enzyme active site, whereas ABP-1...bind plasminogen in a ligand-receptor site." Nevertheless, both Petersen et al. and U.S. Patent #5,679,350 disclose proteins having anti-angiogenic activity. These proteins are indeed receptors for a N-terminal fragment of plasminogen comprising kringle domains 1-4 and/or 5. A receptor is defined as a structural protein molecule on the cell surface or with the cytoplasm that binds to a specific factor, such as a fibrin, antigen or in the instant case a N-terminal fragment of plasminogen comprising the said kringle domains. Likewise a ligand is identified as a molecule that binds to a macromolecule, for example a receptor. The prior art is commensurate within the scope of the claimed subject matter. Whether or not enzymatic activity follows the receptor-ligand interaction, the prior art discloses isolated human proteins having anti-angiogenic activity that are receptor for a N-terminal fragment of plasminogen comprising kringle domains 1-4 and/or 5.

13. Claims 3-8 and 31-33 are free of the art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 3:30 pm. A

message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached on (703)308-4310. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
September 8, 2000

GEETHA P. BANSAL
PRIMARY EXAMINER